# *Variant: NM_001204.7(BMPR2):c.1257A>T (p.Arg419Ser)*

Version: 1.0

*CA350341975*

*425905 (ClinVar)*

**Gene**: BMPR2 (HGNC:659)
**Condition**: pulmonary arterial hypertension (MONDO:0015924)
**Inheritance Mode**: Autosomal dominant inheritance
**UUID:** b13676af-48b9-4741-b597-97d48b933dbf
**Approved on**: 2025-01-03
**Published on**: 2025-01-03

## *HGVS expressions*

**NM_001204.7:c.1257A>T**
NM_001204.7(BMPR2):c.1257A>T (p.Arg419Ser)
NC_000002.12:g.202532713A>T
CM000664.2:g.202532713A>T
NC_000002.11:g.203397436A>T
CM000664.1:g.203397436A>T
NC_000002.10:g.203105681A>T
NG_009363.1:g.161387A>T
ENST00000374580.10:c.1257A>T
ENST00000638587.1:c.1188A>T
ENST00000374574.2:c.1257A>T
ENST00000374580.8:c.1257A>T
NM_001204.6:c.1257A>T

**Uncertain Significance**

**Met criteria codes** 2

PM1 PM2_Supporting

**Not Met criteria codes** 4

PP3 BA1 BS1 BP4

Evidence Links 0

### Expert Panel

Pulmonary Hypertension VCEP

### Criteria Specification Information

**Criteria Specification:** *ClinGen Pulmonary Hypertension Expert Panel Specifications to the ACMG/AMP Variant Interpretation Guidelines for BMPR2 Version 1.1.0*
**Criteria Specification Approval History**
**Criteria Specifications for this VCEP**

Evidence submitted by expert panel

***Pulmonary Hypertension VCEP***

**BMPR2 c.1257A>T is a missense variant predicted to cause substitution of arginine to serine at amino acid position 419 (p.Arg419Ser). The variant is absent from gnomAD v2.1.1 controls and found at a maximum allele frequency of 0.000022 in gnomAD v4.1.0 in the East Asian ancestry group, meeting PM2_supporting criterion of <0.01% (BA1 and BS1 not met). The REVEL score of 0.59 does not meet BP4 (<=0.25) or PP3 (>=0.75) criteria. This variant resides within the critical kinase domain (PM1_moderate met). Co-segregation/case, experimental criteria, and alternative missense variants at the same location were not evaluated due to lack of reported evidence. In summary, this**

**variant meets the criteria to be classified as a variant of uncertain significance for pulmonary arterial hypertension based on the ACMG/AMP criteria applied, as specified by the ClinGen Pulmonary Hypertension VCEP: PM2_supporting, PM1_moderate (VCEP specification version 1.1.0, 1/18/2024).**

**Met criteria codes**

| | | |
|---|---|---|
| **PM1** | ✔ | This variant resides within the critical kinase domain but not is not a known critical residue, so PM1_moderate is met. |
| **PM2_Supporting** | ✔ | The variant is absent from gnomAd v2.1.1 controls and with a maximum allele frequency of 0.000022 in gnomAD v4.1.0 in the East Asian ancestry group, meeting PM2_supporting criterion of <0.01%. |

**Not Met criteria codes**

| | | |
|---|---|---|
| **PP3** | ✖ | REVEL score of 0.59 does not meet BP4 (<=0.25) or PP3 (>=0.75) criteria. |
| **BA1** | ✖ | The variant is absent from gnomAd v2.1.1 controls and with a maximum allele frequency of 0.000022 in gnomAD v4.1.0 in the East Asian ancestry group, meeting PM2_supporting criterion of <0.01%. |
| **BS1** | ✖ | The variant is absent from gnomAd v2.1.1 controls and with a maximum allele frequency of 0.000022 in gnomAD v4.1.0 in the East Asian ancestry group, meeting PM2_supporting criterion of <0.01%. |
| **BP4** | ✖ | REVEL score of 0.59 does not meet BP4 (<=0.25) or PP3 (>=0.75) criteria. |

Curation History

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